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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/541,476	07/06/2005	Craig A Coburn	21310YP	7772

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EXAMINER	
JARRELL, NOBLE E	

ART UNIT	PAPER NUMBER
1609	

MAIL DATE	DELIVERY MODE
06/28/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,476	COBURN ET AL.	
	Examiner	Art Unit	
	Noble Jarrell	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-13* is/are allowed.

6)☒ Claim(s) *14 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :July 6, 2005 and January 31, 2006.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of claims 1-15 in the reply filed on May 14, 2007 is acknowledged.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 15 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabled for compounds of formula I, and their respective ability as beta-secretase inhibitors (page 24, lines 10-13), is not enabled for the prevention or halting of Alzheimer's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

> The factors to be considered in determining whether a disclosure meets the enablement requirements of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in Wands states, "Enablement is not precluded by the necessity for some experimentation, such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue', not 'experimentation'" (*Wands*, 8 USPQ2sd 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations" (*Wands*, 8 USPQ2d 1404). Among these factors are: (1) the nature of the invention; (2) the breadth of the claims; (3) the state of the prior art; (4) the predictability or unpredictability of the art; (5) the relative skill of those in the art; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

(1) The nature of the invention and (2) the breadth of the claims:

The claims are drawn to macrocyclic compounds with ring systems that have benzene rings embedded within the ring system. Applicants state that these compounds can be used to inhibit beta-secretase, and therefore treat and/or prevent Alzheimer's disease and other diseases associated beta-secretase. Thus, the claims taken together with the specification imply the claimed macrocyclic compounds that can treat various cognitive disorders.

(3) The state of the prior art and (4) the predictability or unpredictability of the art:

The compounds encompassed by claim can be considered novel.

(5) The relative skill of those in the art:

One of ordinary skill in the art is experienced in Mitsonobu couplings and amide couplings.

(6) The amount of direction or guidance presented and (7) the presence or absence of working examples:

The specification has provided guidance for preparation of compounds encompassed by formula I, compositions of these compounds in DMSO in four different concentrations (1 mM, 100. μM, 10 μM, and 1 nM) (page 23, line 20), and testing of these compounds as beta-secretase inhibitors. Applicants report that that IC_{50} values for the compounds ranged from 1 nM to 1 μM (page 24, lines 10-14).

However, the specification does not provide guidance for the prevention or halting of Alzheimer's disease. Pulley et al. (US 7,067,507, issued June 27, 2006) state the following (column 2, lines 40-44): "At present there are no effective treatments for halting, preventing, or reversing the progression of Alzheimer's disease. Therefore, there is an urgent need for pharmaceutical agents capable of slowing the progression of Alzheimer's disease and/or preventing it in the first place." This statement conveys a message that Alzheimer's disease has no cure (in other words, no prevention or halting). Thus, applicants are not enabled for the prevention or halting of Alzheimer's disease.

(8) The quantity of experimentation necessary:

Considering the state of the art as discussed by the references above, particularly with regards to the novelty of the compound and the high unpredictability in the art as evidenced therein, and the lack of

guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate in the scope of the claims.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

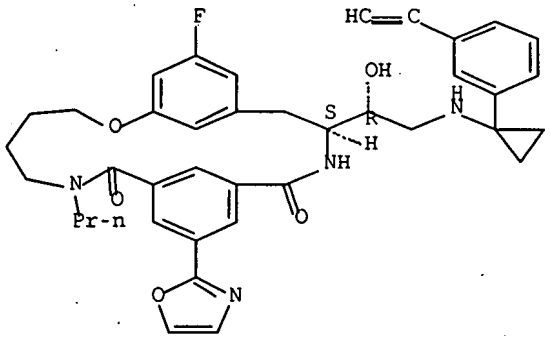
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 14 is unclear as to its intended scope. Such claim language reciting inhibitory activity is generally used to denote a causative factor in determining the process by which a particular disease occurs. Determining whether a given disease responds or not to inhibition of "beta-secretase" involves much experimentation since a negative response from one patient does not mean the drug isn't useful as no drug has 100% effectiveness. Thus what "success rate" determines if a particular compound is effective and how many patients (and dosage regimens) need to be tested? Applicants cite (page 19, (lines 14-23) other diseases than Alzheimer's that are associated with beta-secretase: mild cognitive impairment, Down syndrome, cerebral amyloid angiopathy, degenerative dementia, et al. The test for determining compliance with 35 USC 112, paragraph two, is whether applicants have clearly defined "their" invention not what may be discovered by future research as this type of claim language clearly requires.

Allowable Subject Matter

6. Claim 12 is allowed over the prior art of record.

7. The following is a statement of reasons for the indication of allowable subject matter: Pulley et al. prepare a structure with the registry number 477954-58-8, which is shown below for Applicants' convenience..



This structure does not read on claims 1-11 because fluorine is not allowed on the phenyl ring directly attached to the oxygen, an isopropyl group is not a valid group as a substituent on the nitrogen, and the group for variable R^3 is not valid because alkylamino is not one of the possible groups.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Noble Jarrell whose telephone number is (571) 272-9077. The examiner can normally be reached on Monday-Friday from 7:30 to 6:00. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

NJ

Cecilia J. Tsang
Supervisory Patent Examiner
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